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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/935,703	08/24/2001	Yanggu Shi	PT050P1	9669

22195 7590 06/26/2003

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EXAMINER
RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
1652	8

DATE MAILED: 06/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/935,703	SHI ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12,13,17-20 and 22-42* is/are pending in the application.

4a) Of the above claim(s) *12,13,17-20 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Claims 12-13, 17-20, 22-42 are pending.

It is noted that the examination of the instant application has been assigned to a different Examiner in Group Art Unit 1652.

Applicant's election with traverse of Group I, claims 1-10, 14, 15 drawn in part to the polynucleotide of SEQ ID NO: 2 and a polynucleotide encoding the polypeptide of SEQ ID NO: 7, cancellation of claims 1-11, 14-16, 21, and addition of claims 23-42, in Paper No. 7, filed on 6/2/2002 is acknowledged.

Applicant's traverse is on the ground(s) that while the Examiner has argue that Groups I-VIII are separately classified, with respect to a given sequence, a search of the claims of the groups directed to that sequence would also provide useful information for the claims of the other groups directed to that sequence. It is Applicant's contention that the searches for all these groups would overlap. Applicants also submit that Groups I, II, VI and VII are not separately classified. In regard to the restriction of groups directed to different nucleic acid sequences, Applicants argue that the Examiner has not addressed MPEP 803.04 which states that even when nucleotide sequences encoding different proteins are contained in an application, a reasonable number , normally 10 sequences will be examined in a single application. Therefore, it is Applicant's contention that 5 sequences is not unreasonable in this case. Applicants submit that if the product of Group I is found allowable, the process claims of Group V should be rejoined for examination.

Applicant's arguments have been fully considered but are not found persuasive to overcome the restriction requirement. While it is true that publications containing polynucleotide information such as open reading frame sequences typically disclose the corresponding polypeptide (Group I), it is false to assume that the only source of information about a polypeptide or its antibody is one in which polynucleotide information is disclosed. Similarly, publications which disclose a protein may not necessarily disclose polynucleotides, antibodies or methods of use of such protein or antibody. Therefore, the Examiner must search not only for polynucleotide but also for polypeptide, and antibody information. In regard to the classification of Groups I, II, VI and VII, it is noted that while one class/subclass is indicated, a comprehensive search would require not only class/subclass searches but patented/non-patented literature searches as well as sequence searches. Furthermore, it is noted that a comprehensive class/subclass search would require searching more than just the class/subclass indicated. In regard to the number of sequences that can be examined in a single application, the guidelines set forth in M.P.E.P. § 803.04 clearly indicate that ***up*** to (***not at least***) 10 independent and distinct nucleotide sequences can be examined in a single application. Therefore, the number of nucleotide sequences to be examined in one single application can vary from 1 to 10. However, searching more than one nucleotide sequence per application will place an undue burden upon the Examiner and the Office since the search of sequences is not co-extensive, and would require additional computational time. In view of the fact that a comprehensive search of all Groups and sequences would require sequence searches which are not co-extensive, searches in the patent and non-patented literature, as well as class/subclass searches, an undue burden would be imposed on the Office if all these inventions are examined in a single application. In regard to

the rejoinder of the process claims of Groups V, these claims will be examined according to *In re Ochiai, In re Brouwer* and 35 USC § 103 (b) once the product claims are found allowable.

The requirement is deemed proper and therefore is made FINAL.

Claims 12-13, 17-20 and 22 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Priority

1. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to provisional application No. 60/186,658 filed on 03/03/2000, and 60/189,881 filed on 03/16/2000.

2. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 120 or 121 to PCT/US01/05496 filed on 02/22/2001

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 23-42 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial and specific asserted utility or a well established utility.

The instant claims are directed to the polynucleotide of SEQ ID NO: 2, polynucleotides encoding the polypeptide of SEQ ID NO: 7, polynucleotides encoding polypeptides comprising amino acid residues 1-67 of SEQ ID NO: 7, vectors, host cells and a method of using the polynucleotides.

The specification discloses that the instant polynucleotides encode novel protein tyrosine phosphatase proteins (PTPase; page 1, second paragraph). In page 11, paragraphs 36-38, it is asserted that polynucleotides encoding the polypeptide of SEQ ID NO: 7 share sequence homology with a murine protein tyrosine phosphatase (GenBank accession number BAA23761) and therefore, it is expected that the polypeptide of SEQ ID NO: 7 would share at least some biological activities with members of the tyrosine phosphatase family of proteins. The specification discloses that the polynucleotides and polypeptides of the instant invention are useful reagents for differential identification of the tissue or cell type present in a biological sample and for diagnosis of diseases and conditions such as breast cancer and disorders of the vascular system since a polynucleotide encoding the polypeptide of SEQ ID NO: 7 (GENE NO:1) is expressed in synovial fibroblasts, microvascular endothelial cells and breast cancer tissue.

While Applicants have proposed a function for the polypeptide of SEQ ID NO:7 and for polynucleotides encoding it, and have disclosed uses for these polynucleotides, the instant polynucleotides does not meet the utility requirements for the following reasons.

The polypeptide of SEQ ID NO: 7, which is encoded by the polynucleotide of SEQ ID NO: 2, is only 67 amino acids long. Neel et al. (Current Opinion in Cell Biology 9:193-204, 1997; cited in the specification) teaches that tyrosine phosphatases have at least one catalytic domain of approximately 240 residues (page 193, second column, lines 29-31). Even the closest tyrosine phosphatase homolog disclosed in the specification, i.e. BAA23761 (Ohsugi et al., J. Biol. Chem. 272:33092-33099, 1997), is a 426 amino acid polypeptide. Therefore, in view of the teachings of the art in regard to the catalytic domains of tyrosine phosphatases, it is unlikely

that a polypeptide of only 67 amino acids will display tyrosine phosphatase activity. Absent experimental evidence indicating that the polypeptide of SEQ ID NO: 7 is indeed a tyrosine phosphatase, the asserted utility, i.e. polynucleotide encoding a tyrosine phosphatase, constitutes a utility that requires further research to identify or reasonably confirm a "real world" context of use. See e.g., Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). This type of utility is not considered a "substantial utility" since the instant polynucleotide is suitable only for additional research.

While Applicant's assertion in regard to function may be correct, the asserted function for the polynucleotide of SEQ ID NO: 2 and the polypeptide of SEQ ID NO: 7 is based solely upon sequence alignment analysis and the specification does not provide any empirical evidence that the polypeptide of SEQ ID NO: 7 is a tyrosine phosphatase. The state of the art teaches the unpredictability of assigning function based on structural homology. Bork (Genome Research, 10:348-400, 2000) teaches that protein function is context dependent, and both molecular and cellular aspects must be considered (page 398). The art also shows several examples of variants with high degree of similarity with different function. Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995) teaches that polypeptides of approximately 67% homology to a desaturase from *Arabidopsis* where found to be hydroxylases once tested for activity. Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Broun et al. (Science 282:1315-1317, 1998) teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase to a desaturase.

Witkowski et al. (Biochemistry 38:11643-11650, 1999) teaches that one amino acid substitution transforms a β-ketoacyl synthase into a malonyl. In the instant case, the polynucleotide of SEQ ID NO: 2 is at best 16.8% sequence identical to the polynucleotide (GenBank accession number D64141) encoding the tyrosine phosphatase protein disclosed as GenBank accession number BAA23761 (SPTREMBL accession number O55082). At the amino acid level, the polypeptide of SEQ ID NO: 7 is at best 32.8% overall sequence homologous to the polypeptide disclosed as GenBank accession number BAA23761 and the region of homology is limited to a small portion (15 amino acids) of the mouse tyrosine phosphatase's catalytic domain which is homologous to that of other tyrosine phosphatases (Ohsugi et al., page 33095, Figure 2, legend; residues 187-424). See attached alignments. Therefore, in view of the extremely low sequence identity/homology between the polynucleotide of SEQ ID NO: 2/polypeptide of SEQ ID NO: 7 and the mouse polynucleotide/polypeptide indicated above, one cannot reasonably conclude that Applicant's asserted utility is substantial or well-established. The asserted utility, i.e. polynucleotide encoding a tyrosine phosphatase, particularly in view of the extremely low sequence identity/homology to a tyrosine phosphatase or a polynucleotide encoding a tyrosine phosphatase, constitutes a utility that requires further research to identify or reasonably confirm a "real world" context of use. See e.g., Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). This type of utility is not considered a "substantial utility". Here the instant polynucleotides are suitable only for additional research. Furthermore, even if the claimed polynucleotides encode a tyrosine phosphatase, the specification is silent in regard to its specificity or its substrates. The art teaches that there are at least 3 families of molecules composing the tyrosine phosphatase family. Even the specification teaches that these enzymes

belong to a diverse family of proteins and that they have diverse biological function (page 2, paragraphs 5-6). Thus, in view of the information provided and the teachings of the art, one cannot reasonably conclude that Applicants disclosed a specific and substantial utility for the claimed polynucleotides.

5. Claims 23-42 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112, First Paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 33-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention of claims 33-42 appears to employ novel vectors, i.e. plasmid HATBM23. Since the vectors are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The required plasmids are not fully disclosed, nor have all the sequences required for their construction been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. §

112 may be satisfied by a deposit of the plasmids. The specification does not disclose a repeatable process to obtain the vector and it is not apparent if the DNA sequences are readily available to the public. Accordingly, it is deemed that a deposit of these plasmids should have been made in accordance with 37 CFR 1.801-1.809.

It is noted that Applicants have deposited the organisms but there is no indication in the specification as to public availability. If the deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain/vector has been deposited under the Budapest Treaty and that the strain/vector will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.1809, Applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

a. during pendency of this application, access to the invention will be afforded to the Commissioner upon request;

b. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

c. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and

d. the deposit will be placed if it should ever become unviable.

Conclusion

8. No claim is in condition for allowance.

9. Applicants are requested to submit a clean copy of the pending claims (including amendments, if any) in future written communications to aid in the examination of this application.

10. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
June 24, 2003

REBECCA E. PROUTY
PRIMARY EXAMINER
1600